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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/532,605 | 08/18/2005 | Takehiro Miwa | Q87625 | 9927 |

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| EXAMINER | |
|---|---|
| ARIANI, KADE | |

| ART UNIT | PAPER NUMBER |
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| 1651 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/532,605 | MIWA ET AL. | |
| | Examiner | Art Unit | |
| | KADE ARIANI | 1651 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *6,9,11,17-20,22,24,26,28,30-34,36,38,40 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,9,11,17-20,22,24,26,28,30-34,36,38,40 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## *DETAILED ACTION*

The amendment filed on May 29, 2009, has been received and entered.

Claims 10, 21, 23, 25, 27, 29, 35, 37, 39, 41 have been canceled.

Claims 6, 9, 11, 17-20, 22, 24, 26, 28, 30-34, 36, 38, 40, and 42 are pending in this application and were examined on their merits.

## *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 6, 9-11, and 17-42 under 35 U.S.C. 103(a) as being unpatentable over Shih et al. (US2002/0172989 A1) and in view of Olsen et al. (WO 98/30682-A1), and further in view of Genov et al. (Biochem J, 1982, Vol. 207, p.193-200), is withdrawn due to applicant's amendments to the claims.

Claims 6, 9, 11, 17-20, 22, 24, 26, 28, 30-34, 36, 38, 40, and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shih et al. (US2002/0172989 A1)

and in view of Olsen et al. (WO 98/30682-A1), and further in view of Genov et al. (Biochem J, 1982, Vol. 207, p.193-200).

Claims 6 and 17-20, 22, 24, 26, 28, and 30 are drawn to a method for digesting a protein highly resistant to denaturation and degradation, comprising the step of bringing the protein highly resistant to denaturation and degradation into contact with an enzyme exhibiting an activity of digesting a protein highly resistant to denaturation and degradation and having the following properties, hydrolyzing a peptide bond, MW 31,000, pI 9.3, optimum pH 9.0 to 10.0, optimum temperature for activity 60 to 70ºC, wherein the contacting step is carried out without preheating the subject, exhibiting an activity of 2U/g or more as the activity of digesting a protein highly resistant to denaturation and degradation (determined as an activity of digesting keratin azure), derived from a microorganism belonging to genus *Bacillus*, wherein the enzyme is selected from the group consisting of an enzyme comprising the amino acid sequence of SEQ ID No:2, wherein the protein highly resistant to denaturation and degradation is a pathogenic prion protein, and wherein the contacting step is carried out without preheating the subject at 90ºC or more.

Claims 9, 11, and 31-34, 36, 38, 40 and 42 are drawn to a method for detoxifying a pathologic prion protein, comprising the step of bringing a subject which may be contaminated with a pathological prion protein into contact with an enzyme exhibiting an activity of digesting a protein highly resistant to denaturation and degradation and having the following properties, hydrolyzing a peptide bond, MW 31,000, pI 9.3, optimum pH 9.0 to 10.0, optimum temperature for activity 60 to 70ºC, wherein the

contacting step is carried out without preheating the subject, exhibiting an activity of 2U/g or more as the activity of digesting a protein highly resistant to denaturation and degradation (determined as an activity of digesting keratin azure), derived from a microorganism belonging to genus *Bacillus*, wherein the enzyme is selected from the group consisting of an enzyme comprising the amino acid sequence of SEQ ID No:2, wherein the protein highly resistant to denaturation and degradation is a pathogenic prion protein, wherein the contacting step is carried out without preheating the subject, and wherein the contacting step is carried out without preheating the subject at 90ºC or more.

Shih teaches a method for digesting of infectious prion proteins comprising the step of bringing the protein into contact with an enzyme, the enzyme is derived from a *Bacillus* (*Bacillus licheniformis)* (Abstract, Page 1 0002, 0006,0010, and Page 3 0054), and the contacting step is carried out without preheating the subject at 90ºC or more (page 2 0031). Shih teaches it will be recognized that any of a wide variety of proteases may be employed in the practice of the invention and that the choice of specific proteolytic enzyme will affect the choice of temperature that is used to carry the proteolytic degradation, as well as the choice of any elevate temperature treatment of the tissue before its exposure to the proteolytic enzyme (Page 3, 0046). Shih further teach proteolytic enzymes include subtilisins and keratinase enzymes, and active fragments of the enzyme (Page 3 0053-0054). Shih teaches the method achieves a substantial advance in the art, permitting nutritional use of a material that would otherwise, in the absence of the treatment, constitute a biological hazard, and to avoid

costs and infrastructure requirements for incineration and disposal of infected or contaminated animal tissue (page 4 0071). Shih further teaches a method for reduction of infective prion protein (a method for detoxifying a pathologic prion protein) (page 6 Claim 1). Shih teaches the enzyme is a serine protease (p.5 0086).

Shih does not teach wherein the contacting step is carried out without preheating the protein, the enzyme exhibiting, MW 31,000, pI 9.3, optimum pH 9.0 to 10.0, optimum temperature for activity 60 to 70ºC, exhibiting an activity of 2U/g or more as the activity of digesting a protein highly resistant to denaturation and degradation (determined as an activity of digesting keratin azure), an enzyme comprising the amino acid sequences of SEQ ID NO: 2. However, Shih teaches it will be recognized that any of a wide variety of proteases may be employed in the practice of the invention and that the choice of specific proteolytic enzyme will affect the choice of temperature that is used to carry the proteolytic degradation, as well as the choice of any elevated temperature treatment of the tissue before its exposure to the proteolytic enzyme (Page 3, 0046).

Olsen et al. teach an enzyme comprising the amino acid sequences of SEQ ID NO: 2, (subtilisin DY) with MW of 27,000 (p.19, line 10), the enzyme taught by Olsen et al. is same as the corresponding element disclosed in the specification, therefore it possesses the claimed functional characteristics of the claimed enzyme, since an enzyme cannot be separated from its properties, the claimed properties, in this case, activity and substrate specificity, MW, pI, optimum pH, and optimum temperature, etc.

are necessarily present. Olsen et al. further teach the enzyme subtilisin DY (protease) digest a protein highly resistant to denaturation (remove keratinous material) (p. 18, lines 3 and Table 2. column 6th row, and p.20 lines 29-30).

Genov et al. teach subtilisin DY (derived from a Bacillus) is an alkaline serine protease, and displays optimum proteolytic activity at a pH about 10 (see Genov et al. Introduction 1st column last paragraph and 2nd column 1st paragraph).

Therefore, a person of ordinary skill in the art at the time the invention was made would have been motivated to try and to use the enzyme as taught by Olsen et al. in the method as taught by Shih to provide a method for digesting a protein highly resistant to denaturation and degradation and a method for detoxifying a pathologic prion protein with a reasonable expectation of success, because Shih teaches subtilisins can be used in the method for digesting of infectious prion proteins and for detoxifying a pathologic prion protein, and because Olsen et al. teach an enzyme comprising the amino acid sequences of SEQ ID NO: 2 digest a protein highly resistant to denaturation.

***Answer to Arguments***

Applicant's arguments filed on 05/29//2009 have been fully considered but they are not persuasive.

Applicant argues that the method of Shih requires a pretreatment step to cook the tissue at a temperature from about 100°C to about 150°C

However, as mentioned immediately above, Shih teaches it will be recognized that any of a wide variety of proteases may be employed in the practice of the invention and that the choice of specific proteolytic enzyme will affect the choice of temperature that is used to carry the proteolytic degradation, as well as the choice of any elevated temperature treatment of the tissue before its exposure to the proteolytic enzyme (Page 3, 0046). Therefore, Shih suggests the treatment temperature (preheating) of the tissue before its exposure to the proteolytic enzyme would have depended on the proteolytic activity of the enzyme, and a person of ordinary skill in the art at the time the invention was made would have recognized that a preheating step might not be necessary in Shih's method.

Applicant alleges that the presently claimed method results in unexpectedly superior enzyme digestion without preheating a subject tissue, and the unexpected properties of the enzyme are evidence of the non-obviousness, because Applicant have shown in Example 8 and figure 6 of the present application that under such conditions , the claimed enzyme provides unexpectedly superior digestion of prion proteins in comparison to the keratinase derived from *B. licheniformis* PWD-1 as described in Shih (see Remarks p.11 last paragraph).

Applicant's has demonstrated that the pathogenic prion protein was not digested by the enzyme compositions B-E (enzyme compositions of strains PWD-1 and DSM-8782) without preheating a subject tissue, but was completely digested by the enzyme composition A (enzyme composition of strain FERM BP-08487). However, the evidence is not sufficient to rebut prima facie case of obviousness based on prior art which

specifically taught the use of proteolytic enzymes including subtilisins in the method for digesting of infectious prion proteins and for detoxifying a pathologic prion protein, and that an enzyme comprising the amino acid sequences of SEQ ID NO: 2 digest a protein highly resistant to denaturation, and that the treatment temperature (preheating) of the tissue before its exposure to the proteolytic enzyme would have depended on the proteolytic activity of the enzyme. Therefore, the evidence does not show that digestion of infectious prion proteins would have been unexpected, and it is not sufficient to establish the nonobviousness, because it is not sufficient to establish that a person of ordinary skill in the art at the time the invention was made would have not been motivated to use the enzyme taught by the prior art in the method of Shih et al. to provide a method for digesting infectious prion proteins and a method for detoxifying a pathologic prion protein with a reasonable expectation of success.

## ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kade Ariani whose telephone number is (571) 272-6083. The examiner can normally be reached on 9:00 am to 5:30 pm EST Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kade Ariani
Examiner
Art Unit 1651

/Leon B Lankford/
Primary Examiner, Art Unit 1651